WEB WATCH

Collating immune genes

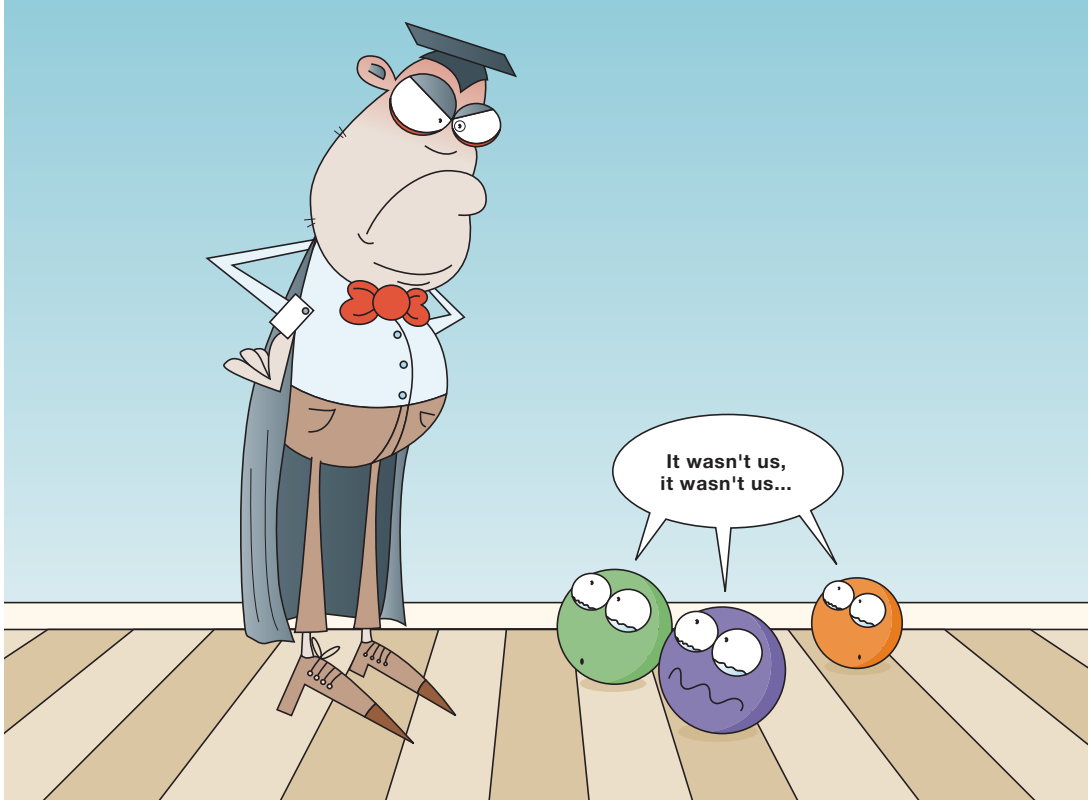
- http://www.immunegene.org

With the complete human-genome sequence now available and large numbers of researchers using DNA-microarray analysis to study the immune system, databases that allow investigators to identify genes that are of sufficient interest to study in more detail are crucial research tools.

The Immunogenetic Related Information Source (IRIS) is an online database run by researchers in Professor John Trowsdale's laboratory at the University of Cambridge. It includes more than 1,500 human genes, ~7% of the human genome, all of which are known to produce a functional transcript that encodes a protein shown to have at least one immune characteristic. In this context, an immune characteristic is defined as the following: a known or putative function in innate or adaptive immunity, participation in the development or maturation of the immune system, induction by an immunomodulator, participation in a signalling pathway that results in the induction of genes involved in host defence, direct interaction with a pathogen or pathogen-derived molecule, or expression mainly in immune tissues.

For each gene, information is provided about its chromosomal location and its nucleotide and protein sequence, as well its proposed immune function. The web site allows users to search for an individual gene by its official HUGO (Human Gene Organisation) gene name or to search for genes at a particular chromosomal location or with a specific proposed function. This organization of human immune-function genes should be of particular interest to researchers studying the genetics of the immune response and immune-related diseases.

Karen Honey



ANTIBODY RESPONSES

Don't blame the B cells

As we get older, our antibody responses gradually become weaker and less long-lived, leaving many elderly individuals susceptible to infection with viruses such as influenza — despite having been vaccinated against them. New research published in *The Journal of Experimental Medicine* lets the most likely culprit, B cells, off the hook and indicates that the fault may lie instead with T cells.

To confirm previous findings, the authors immunized young and aged mice with an antigen conjugate of nitrophenyl and pigeon cytochrome *c* (NP–PCC); the aged mice had fewer NP-specific B cells, of which a smaller proportion differentiated into a germinal-centre phenotype, and had lower serum titres of NP-specific IgG, indicating an age-related defect in B-cell proliferation, differentiation and antibody production. But, because the number of naive $CD4^+$ T helper cells, which are crucial for germinal-centre reactions, could not be determined in these mice and because there is also known to be a decrease in the number of naive $CD4^+$ T cells with age, the authors set out to determine which lymphocyte population is responsible for the defective antibody response.

AND T-cell receptor (TCR)-transgenic $CD4^+$ T cells, which are specific for PCC, were transferred into CD4-deficient recipients, which have no T helper cells of their own. When AND T cells from young mice were transferred to young CD4-deficient hosts immunized with NP–PCC, NP-specific B cells proliferated and differentiated to a germinal-centre phenotype. However, when aged donor cells were transferred to young immunized mice, B-cell responses were significantly reduced in terms of proliferation, differentiation, and production of NP-specific IgG, even when the number of transferred cells was increased. In the reverse experiment, when donor cells from young mice were transferred to young or aged immunized hosts, there was no difference in the proliferation, differentiation or IgG production of NP-specific B cells. This shows that it is age-related changes in the $CD4^+$ T-cell population, rather than in the B-cell population, that determine the NP-specific antibody response.

Both young and aged $CD4^+$ T cells were shown to migrate efficiently into germinal centres, correlating with similar levels of expression of the chemokine receptor CXCR5. There was also no difference in the cell-surface expression levels of CD28 or CD134 (OX40) between young and aged $CD4^+$ T cells, both of which are thought to be required for cognate function. However, there was a marked reduction in the level of expression of CD154 (also known as CD40 ligand) by aged activated T helper cells. Because CD40–CD154 interactions between B and T cells are required for germinal-centre formation and antibody class switching, this could explain the poor antibody responses in the presence of aged $CD4^+$ T cells.

Kirsty Minton

References and links

ORIGINAL RESEARCH PAPER Eaton, S. M., Burns, E. M., Kusser, K., Randall, T. D. & Haynes, L. Age-related defects in CD4 T cell cognate helper function lead to reductions in humoral responses. *J. Exp. Med.* **200**, 1613–1622 (2004).

FURTHER READING Linton, P. J. & Dorshkind, K. Age-related changes in lymphocyte development and function. *Nature Immunol.* **5**, 133–139 (2004).